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Effects of atropine on blood gas parameters and pulmonary shunt fraction

Atropine and pulmonary shunt fraction

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Abstract

Aim: Atropine has been used for a long time in anesthesia management to inhibit salivary and bronchial secretions and laryngospasm before administration of an anesthetic agent. The objective of this study was to investigate the effects of atropine blood gas parameters and pulmonary shunt fraction for the first time in the literature.

Material and Methods: A total of 24 patients aged 20-75 years, hospitalized in the intensive care unit under mechanical ventilation were included in the study. 0.01 mg/kg atropine was administered intravenously and arterial and venous blood gas samples were taken at 15, 45 and 90 minutes, and the shunts were calculated. pH, PO2, PCO2, H+, HCO3 and SO2 values were measured and recorded. In addition, pulmonary shunt (QS/QT) fraction was calculated at 0, 15, 45 and 90 minutes.

Results: pAO2 values were statistically significantly higher at the 15th minute (109.63±7.95) compared to the 0th minute (107.00±5.99) (p=0.006) and 90th minutes (107.55±8.28) (p=0.022). CaO2 values were statistically significantly lower at the 45th minute (13.70±1.43) compared to the 0th minute (14.70±1.66) (p=0.013) and 90th minute (14.40±1.59) (p=0.008). Shunt (Qs/Qt) values were statistically significantly lower at the 45th minute (0.12±0.17) compared to the 0th minute (0.04±0.04) (p=0.040) and 90th minutes (0.07±0.10) (p=0.007).

Discussion: Administration of atropine significantly increased the pulmonary shunt, regardless of the current pathology, mechanical ventilation and treatment applied. Atropine increased the shunt at the maximum level, especially at the 45th minute. In this study, the shunt emerged as the gold standard in determining the treatment modality.

Keywords

Anesthesia, Atropine, Blood Gas, Pulmonary Shunt, QS/QT Fraction

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Introduction

Atropine is a commonly used anticholinergic medication used in the emergency department to reserve bradycardia and to dry pulmonary secretion or as a mydriatic agent [1]. This drug provides an unusual rearrangement of some determinants of pulmonary capillary function (available at: https://www.ncbi.nlm.nih.gov/books/NBK470551/). It is also indicated in post-intubation-related bradycardia. Atropine has been used for a long time in anesthesia management to inhibit salivary and bronchial secretions and laryngospasm before administration of an anesthetic agent. It has been reported that administration of atropine before induction of anesthesia can significantly increase heart rate, mean arterial pressure and cardiac index [2]. In addition, atropine is easily available and more cost effective compared to vasopressors and IV fluids. It has been reported that prophylactic atropine administration reduced the incidence of hypotension and bradycardia [3].

Blood gas management is critical in anesthetized patients with maintaining proper acid-base and electrolyte balances in order to optimize the body's functions while compromised under anesthesia [4]. Monitoring blood gases during anesthetic management is crucial to prevent hypothermia, hypoxia and acidosis [5]. In a rat model, atropine was found to decrease pulmonary gas exchange in a dose-dependent fashion [1].

General anesthesia causes impairment in pulmonary blood gas exchange and respiratory parameters even in people with healthy lungs [6]. Pulmonary compliance decreases and pulmonary shunt fraction increases during general anesthesia because of the development of atelectasis [7]. It has been shown that a progressive decrease in respiratory rate coupled with increasing CO2 removal in mechanically ventilated healthy pigs under general anesthesia is associated with the development of lung atelectasis, higher shunt, and poorer oxygenation [8].

The objective of this study was to investigate the effects of atropine blood gas parameters and pulmonary shunt fraction for the first time in the literature.

Material and Methods

This randomized controlled study was conducted in the intensive care unit of our hospital. Before the beginning, the study protocol was approved by the local ethics committee of our hospital. All patients were informed about the objectives of the study in detail and gave written informed consent. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments.

A total of 24 patients aged 20-75 years, hospitalized in the intensive care unit under mechanical ventilation were included in the study. Patients with poor general condition, SpO2<90%, mean arterial blood pressure <60 mmHg, hemodynamically unstable, receiving inotropic support, diagnosed with ARDS, hypovolemic shock, undergoing hemodialysis, and FiO2 value set to >60% on mechanical ventilator were excluded from the study.

All patients were routinely monitored with electrocardiogram (ECG), peripheral oxygen saturation (Drager infinity delta MS13466E539D, USA), and heart rate. After the Allen test was applied, arterial cannulation was performed from the right or left radial artery, and arterial blood pressure was continuously monitored. Blood gas samples were collected through this cannula. Shunt and blood gas values of the patients were studied with Radiometer ABL 800 FLEX blood gas measurement device. pH, PO2, PCO2, H+, HCO3 and SO2 values were measured and recorded. In addition, hemoglobin values, temperatures, and barometric pressures of the patients at the time of measurement were also recorded. Alveolar oxygen pressures were calculated using the following formula: PAO2=PIO2 -(PaCO2/RQ). Oxygen content values were calculated using the following formulas:

CaO2 (ml/dL) = Hb(g/dL) x 1.34(mlO2 /gHb) x SaO2 (%) + (0.003 x PaO2)

CcO2(ml/dL) = Hb(g/dL) x 1.34(mlO2 /gHb) x ScO2 (%) + (0.003 x PAO2) (ScO2 = 1)

CvO(ml/dL) = Hb(g/dL) x 1.34(mlO2 /gHb) x SvO2 (%) + (0.003 x PvO2)

Shunt values were calculated using the following formula: Qs/Qt = CcO2-CaO2 / CcO2-CvO2

First of all, the patients' orotracheal aspiration procedures were performed, arterial and venous blood gases were sampled, and their shunts were measured at the same time. Afterwards, 0.01 mg/kg atropine was administered intravenously and arterial and venous blood gas samples were taken at 15, 45 and 90 minutes, and the shunts were calculated. The study was terminated in patients whose mean arterial pressure deteriorated by more than 30% and SpO2 value fell below 90% during this period. Ventilation modes of the patients during the study were IPPV, BIPAP, CPAP, ASB, and no mode changes were made during the study. pH, PaO2, PaCO2, SaO2 values were determined in arterial and venous blood gases of the patients and Qs/Qt values were determined before and after atropine administration, and all values were compared.

Statistical Analysis

Data obtained in this study were statistically analyzed using the SPSS version 25.0 (SPSS, Statistical Package for Social Science, IBM Inc., Armonk, NY, USA) statistical software. Analysis of variance and Bonferroni tests were used for repeated measurements in comparisons. P<0.05 values were considered statistically significant.

Results

PaO2, PaCO2, pH, pAO2, CcO2, CaO2, CvO2 and Qs/Qt values were measured at 0, 15, 45 and 90 minutes. Accordingly, PaO2 value did not significantly change between minutes 0 and 90 (p=0.264). In addition, there was no statistically significant difference between PaO2 values measured at 0, 15, 45 and 90 minutes (p>0.05).

PaCO2 value did not significantly change between minutes 0 and 90 (p=0.218). In addition, there was no statistically significant difference between PaCO2 values measured at 0, 15, 45 and 90 minutes (p>0.05).

pH value did not significantly change between minutes 0 and 90 (p=0.332). In addition, there was no statistically significant difference between pH values measured at 0, 15, 45 and 90 minutes (p>0.05).

pAO2 values were statistically significantly higher at the 15th minute (109.63±7.95) compared to the 0th minute (107.00±5.99) (p=0.006) and 90th minute (107.55±8.28) (p=0.022). There was no statistically significant difference

Table 1. Arterial blood gas components measured at different time

	0th minute		15th minute		45th minute		90th minute		p value
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	
PaO2	115.30	31.12	121.58	32.70	116.12	27.63	119.76	26.3	0.264
PaCO2	35.29	4.03	34.19	5.19	35.01	4.94	35.24	5.90	0.218
pH	7.47	0.06	7.48	0.07	7.47	0.07	7.48	0.06	0.332
pAO2	107.00	5.99	109.63	7.95	108.66	7.85	107.55	8.28	0.042

Table 2. Shunt components measured at different time points

	0th minute		15th minute		45th minute		90th minute		p value
	Mean	± SD	Mean	±SD	Mean	± SD	Mean	± SD	
CcO2	14.87	1.65	14.15	1.26	13.95	1.36	14.58	1.55	0.122
CaO2	14.70	1.66	13.95	1.25	13.70	1.43	14.40	1.59	0.050
CvO2	12.29	2.14	11.33	1.76	11.23	1.58	11.88	1.98	0.241

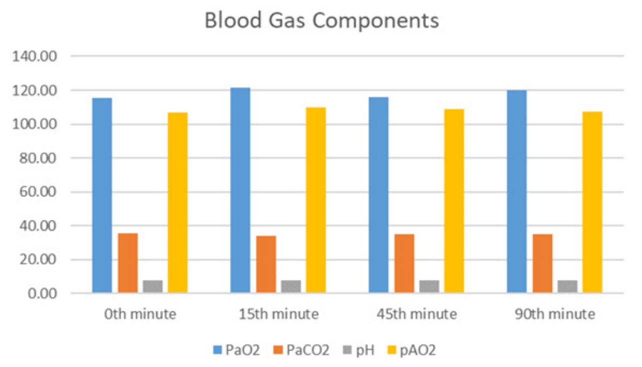

Figure 1. Blood gas components

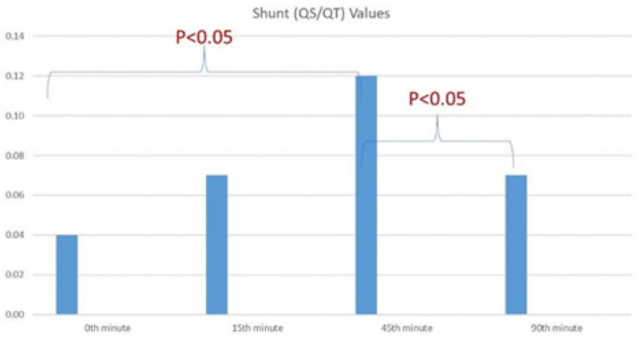

Figure 2. QS/QT fraction measured at different time points

between other measurement time points.

PaO2, PaCO2, pH, and pAO2 values measured at 0, 15, 45 and 90 minutes are shown in Table 1 and Figure 1.

CcO2 value did not significantly change between minutes 0 and 90 (p=0.122). In addition, there was no statistically significant difference between CcO2 values measured at 0, 15, 45 and 90 minutes (p>0.05).

CaO2 values were statistically significantly lower at the 45th minute (13.70±1.43) compared to the 0th minute (14.70±1.66) (p=0.013) and 90th minute (14.40±1.59) (p=0.008). There was no statistically significant difference between other measurement time points.

CvO2 value did not significantly change between minutes 0 and 90 (p=0.251). In addition, there was no statistically significant difference between CcO2 values measured at 0, 15, 45 and 90 minutes (p>0.05).

Shunt (Qs/Qt) values were statistically significantly lower at the 45th minute (0.12±0.17) compared to the 0th minute (0.04±0.04) (p=0.040) and 90th minute (0.07±0.10) (p=0.007). There was no statistically significant difference between other measurement time points.

Shunt components and QS/QT values are shown in Table 2. Shunt values calculated at different time points are shown in Figure 2.

Discussion

It is useful to know some parameters in evaluating the patient's lung functions, determining the need for mechanical ventilation, providing weaning success and optimal mechanical support [9]. Physiological shunt fraction (Qs/Qt) is the gold standard for assessing pulmonary gas exchange [10]. However, several alternative parameters are also used such as P(A-a)O2, PaO2/FiO2, respiratory index (A-a)DO2/PaO2 and A-a) DO2 [11]. On the other hand, another oxygenation index, PaO2/PAO2, overrides PaO2/FiO2, especially when a significant portion of the venous mixture is shunted [12]. It has been shown that the calculation of the shunt is more reliable than (A-a) DO2 even in varying conditions (available at: https://pubmed.ncbi.nlm.nih.gov/31424737/).

In a study by Nirmalan et al. to determine the effect of pulmonary oxygen transfer on changes in arterial and mixed venous oxygen content difference in a lung model with ARDS, patients were evaluated using Qs/Qt, CcO2-CaO2 and PaO2/FiO2 indexes. In this study, it was concluded that Qs/Qt measurement involves the true shunt and V/Q mismatch may have minimal effect in this fraction [13].

The use of atropine for clinical and experimental purposes has been well established. However, few studies have recorded acute effects of these agents on arterial oxygen levels and pulmonary shunt. We attributed this to the transient effect of the administration of atropine. Ali et al. demonstrated that premedication with atropine decreases the incidence of respiratory problems [14].

In the present study, we investigated the effect of atropine infusion on blood gas parameters and pulmonary shunt for the first time. No statistically significant change was found in PaO2, pH and PaCO2 values measured at 0, 15, 45 and 90 minutes following atropine premedication. In their rat model, Gaspari et al. found an abrupt and marked heterogeneity of pulmonary blood flow following atropine treatment [15]. They reported that atropine was found to decrease pulmonary gas exchange in a dose-dependent fashion in this model. Since our study is the first on this issue in humans, we could not accurately compare our results with other studies.

Studies have shown a significant correlation between (A-a) DO2 and shunt [16]. Elliott et al. reported no significant effect of atropine on (A-a)DO2 [17]. However, we think that the QS/QT fraction is more reliable because it involves more content. Stickland et al. stated that increasing heart rate with exercise increases the physiological shunt in the lung [18]. Various hypotheses have been proposed for atropine to increase the pulmonary shunt fraction (Qs/Qt). According to the capillary opening theory, an increase in pulmonary blood flow causes an increase in pulmonary microvascular pressure, leading to shunt by providing arterial-venous vessel opening. Atropine increases the distribution of blood from the lung to the shunt [19].

In line with the literature, in our study, we found that intrapulmonary shunt increased in patients who were administered atropine, that is, in whom vagal stimulation was suppressed, regardless of the existing pathology, mechanical ventilation and treatment. We found that the Qs/Qt ratio increased after intravenous administration of atropine, and this increase was statistically significant at 45 and 90 minutes compared to 0 minutes ($p<0.05$, $p<0.01$) and at other time points, although the Qs/Qt ratio increased, it was not statistically significant. We attributed this to the decrease in CaO2 levels, because CaO2 values were found to be significantly lower at 45 minutes compared to 0 minutes and 90 minutes. In addition, the pAO2 level was found to be significantly higher at the 15th minute after atropine administration compared to the period before atropine administration and 90th minute after atropine administration.

In our study, we found that there was no significant change in PaO2 and pH levels, while PCO2 levels were at acceptable levels. There was no significant change in CcO2 and CvO2 levels either.

Study Limitations

Main limitations of this study are the small number of patients and being conducted in an intensive care unit of a single center. Blood gas parameters and pulmonary shunt could be measured at different doses of atropine. On the other hand, the prospective nature of the study and the fact that it was the first study on the effects of atropine administration on blood gas components and shunt are its strengths. Further randomized controlled prospective studies with a larger series of patients are needed to support our findings.

Conclusion

In this study, we found that the administration of atropine significantly increased the pulmonary shunt, regardless of the current pathology, mechanical ventilation and treatment applied. Atropine increased the shunt at the maximum level, especially at the 45th minute. We observed that the pulmonary shunt started to decrease from the 45th minute onwards, but did not decrease to the level before atropine administration even at the 90th minute, the last time we measured. We observed that the CaO2 levels were significantly lower at the 45th minute than at 0 and 90 minutes, which we attributed to the increase in the Qs/Qt fraction. There was no significant change in pH and PaO2 levels, while a change in PaCO2 levels was within normal limits. In this study, the shunt emerged as the gold standard in determining the treatment modality.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest
The authors declare no conflict of interest.

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